

Attorney Docket No. IVD 1087

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
CASELLAS, et al.

Serial No.: 09/831,720

Filed: May 14, 2001

Group Art Unit: 1651

Examiner: Kailash C. Srivastava

For: USE OF A SUBSTANCE BINDING
WITH THE PERIPHERAL
BENZODIAZEPIN RECEPTOR FOR
TREATING SKIN STRESS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

RESPONSE

This is a response to the Office Action mailed April 22, 2003 (Paper No. 13) setting a three-month shortened period for reply expiring July 22, 2003. Pursuant to the Petition for Extension of Time under 37 C.F.R. 1.136(a) submitted herewith, the period for reply is extended three months to expire October 22, 2003. This response is therefore timely filed.

Claims 16-41 are in the application.

Claims 18, 28, 37, and 39-41 are withdrawn from consideration as drawn to non-elected subject matter.

Claims 20, 30, and 38 are rejected under 35 U.S.C. § 112, first paragraph, apparently on the grounds that the deposits of strains SRL 4988, 5186, and 5189 fail to meet the criteria set forth in 37 C.F.R. 1.801-1.89.

The rejection is respectfully traversed, and reconsideration and withdrawal thereof are requested. As set forth at page 12 of Applicants' specification, the deposits were made at the Collection Nationale de Cultures de Micro-organismes (CNMC) of the

CERTIFICATE UNDER 37 C.F.R. 1.8(a)
I hereby certify that this correspondence is being deposited on the date indicated below with the United States Postal Service as first class mail addressed to:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Geraldine A. Sla
Name

10/21/03
Date

RECEIVED

OCT 31 2003

TECH CENTER 1600/2900

Institut Pasteur in France on August 27, 1999. The CNMC of the Institut Pasteur is an International Depository Authority (IDA) as established under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (M.P.E.P. 2405), and the deposits were made well in advance of the November 10, 1999, international filing date to which the instant application is entitled. Accordingly, the deposits meet all requirements of 37 C.F.R. 1.801-1.809, and Applicants' specification fully meets the requirements of 35 U.S.C. § 112. The rejection of claims 20, 30, and 38 should therefore be withdrawn.

Claims 16, 17, 19-27, 29-36, and 38 are rejected under 35 U.S.C. § 103(a) as obvious over Friedman et al, U.S. Patent 6,004,556, and Glick et al, published U.S. Patent Application 2001/0016583 in view of Komatsu, U.S. Patent 4,011,140, and Higashide et al, JP 54073195. It is the Examiner's position that Friedman et al disclose at column 3, lines 15-27, the topical application of a composition comprising benzodiazepine and a retinoid to treat a skin condition having dermatological diseases/conditions (e.g., psoriasis, atopic dermatitis); that Glick et al teach at paragraph 0015, lines 1-7, that benzodiazepines have an affinity to peripheral benzodiazepine receptors; and that it would therefore have been obvious to one of ordinary skill in the art at the time the invention was made that benzodiazepine is a peripheral benzodiazepine receptor agonist and the artisan would have topically administered a composition comprising benzodiazepine and retinoid to treat cutaneous stress in an individual based on the teachings of Friedman et al and Glick et al, because Glick et al teaches that benzodiazepine is a peripheral benzodiazepine receptor agonist and Friedman et al teach a topical composition, and a method to treat cutaneous stress by topically administering a composition comprising benzodiazepine and retinoid.

The Examiner further notes that Higashide et al, at lines 4-6 of the Abstract, teach that tobramycin having a benzodiazepine structure is produced by culturing *Nocardia* and that Komatsu, at lines 1-9 of the Abstract, teaches that *Streptomyces* fermentatively produces benzodiazepines, and concludes that one having ordinary skill in the art would have been motivated to modify the teachings of Friedman et al, in view of the teachings of Glick et al, Komatsu, and Higashide et al, because Friedman et al teach a topical composition comprising benzodiazepine and retinoid and a method to administer said

composition to treat cutaneous stress and Glick et al teach that benzodiazepine is a peripheral benzodiazepine receptor agonist. Glick et al further teach administration of a topical composition comprising benzodiazepine to ameliorate dysfunctional cell death and Komatsu and Higashide et al teach fermentative production of benzodiazepine through fermentation of *Streptomyces* and *Nocardia*, respectively. Applicants disagree.

A fair reading of the primary Friedman et al reference does not teach the topical application of a composition comprising benzodiazepine and retinoid to treat a skin condition. Friedman et al is directed to a method of obtaining enhanced topical and/or transdermal systemic effects using emulsions or dispersions of submicron droplets. At column 3, lines 15-27, specifically relied upon by the Examiner, benzodiazepines are included with such drugs as barbiturates, phenothiazines, nifedipine, verapamil, etc., which are intended to exert systemic effects whereas, as stated at lines 26-29, “when...used to treat a skin condition, the active ingredient may be Vitamin A, Vitamin E, a retinoid, a carotene or benzoyl peroxide, and is applied to alleviate, reduce, or prevent dermatological conditions and diseases...” Clearly then, a benzodiazepine is an example of a drug that can be administered systemically by transdermal absorption. Thus, at column 7, lines 9-22, it is stated that benzodiazepines are suitable drugs for systemic effects whereas for cosmetic effects, the active ingredient might be Vitamin A, Vitamin E, a polyunsaturated fatty acid, retinoids, carotenes, or benzoyl peroxide. Moreover, Examples 1-16 relate to various submicron diazepam cream preparations and the systemic tranquilizing effect produced by the topical application thereof. Nowhere does the reference teach the use of any peripheral benzodiazepine receptor ligand for the treatment of cutaneous stress. Nor does it contain any suggestion that such a compound might be useful in that indication.

Glick et al is directed to a certain series of benzodiazepines, which do not bind to central benzodiazepine receptors and have a low affinity for peripheral benzodiazepine receptors. The compounds are stated to be useful in treating conditions associated with dysregulation of the process of all death. Nowhere does the reference teach or suggest that the disclosed benzodiazepines would be useful in treating cutaneous stress. The Examiner relies on Glick et al as teaching that “benzodiazepine is a peripheral benzodiazepine receptor agonist” which teaching is absent in Friedman. In fact, the term

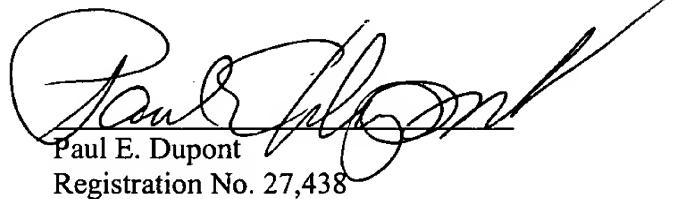
“benzodiazepine” refers to a large class of compounds characterized by a common benzodiazepine nucleus. Some benzodiazepines are selective ligands for the central benzodiazepine receptors whereas others are selective for the peripheral benzodiazepine receptors. Some are ligands for both receptors and some are ligands for neither as noted at page 8, lines 10-15, Applicants’ specification. Thus, the disclosure in Glick et al that a certain class of benzodiazepines have a low affinity for peripheral benzodiazepine receptors adds nothing to Friedman and does nothing to cure the fundamental deficiency of Friedman which is that it fails to teach or suggest the use of any benzodiazepine let alone a peripheral benzodiazepine receptor ligand for the treatment of cutaneous stress.

The Higashide and Komatsu references, which are cited for teaching that certain benzodiazepines having antibacterial and/or antitumor activity can be obtained by fermentation, add nothing to Friedman and Glick. Nowhere is there any mention that the disclosed benzodiazepine molecules bind to any benzodiazepine receptor ligand or can be used to treat cutaneous stress.

In view of the foregoing, it is submitted that the cited references taken individually or in any combination would not have suggested Applicants’ claimed invention.

There being no remaining issues, this application is believed in condition for allowance and such action is earnestly solicited.

Respectfully submitted,



Paul E. Dupont
Registration No. 27,438

Dated: 10/21/03
Sanofi-Synthelabo Inc.
Patent Department
9 Great Valley Parkway
P.O. Box 3026
Malvern, PA 19355
Tel.: (610) 889-6338
Fax: (610) 889-8799